PATENT

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE
BEFORE THE BOARD OF PATENT APPEALS
AND INTERFERENCES

In re application of:	§	**ATTY DCKT NO:** FWLPAT019US
Binie V. Lipps	§	
Frederick W. Lipps	§	**Art Unit:** 1642
	§	
Serial No.: 10/716,982	§	
	§	**Examiner:** Reddig, Peter J.
Filed: November 19, 2003	§	
	§	
For: Saliva test for early diagnosis of cancers	§	

Commissioner for Patents
P.O. Box 1450
Alexandria, VA 22313-1450

REPLY BRIEF

This reply brief is submitted in response to an Examiner's Answer mailed April 10, 2009.

All arguments in Appellants' Brief on Appeal are incorporated by reference herein.

Oral hearing is waived. No fees are seen due.

STATUS OF AMENDMENTS

An amendment after final rejection entered June 23, 2008 which canceled claim 18 and amended claim 24 to obviate a rejection under 35 USC 112, second paragraph has been entered per the advisory action dated September 4, 2008 and the claims as reproduced in the appendix incorporate the amendment.

GROUNDS OF REJECTION TO BE REVIEWED

Rejection 1: Nonenablement

Claims 1-3, 8-12, 16-18, 20 and 24 stand rejected under 35 USC 112, first paragraph, for failure to comply with the enablement requirement, as set forth in the Final Rejection dated April 14, 2008, section 6, pages 3-10, and the Advisory Action dated September 4, 2008 page 2.

Rejection 2: Lack of written description

Claims 1-3, 8-12, 16-18, 20 and 24 stand rejected for failure to comply with the written description requirement, as set forth in the Final Rejection dated April 14, 2008, section 7, pages 10-12, and the Advisory Action dated September 4, 2008 page 2.

STATEMENT OF FACTS

The invention relates to screening for early cancers by using a noninvasive saliva test.

The screening test, which is non-specific for the type of cancer, is conducted by obtaining a saliva specimen from a person to be screened and forming it into a saliva sample. The saliva sample is then brought together with a reagent containing polyclonal antibodies made against a mixture of plurality of proteonic cancer markers from different types of cancer cells to form an assay sample. A determination is then made, for example, by ELISA, as to whether an immunological reaction has occurred in the assay sample. A strong enough immunological reaction is indicative of a positive screening test, and followup testing would be indicated.

ARGUMENT

Rejection 1: Nonenablement

Claims 1-3, 8-12, 16-18, 20 and 24 stand rejected as stated on pages 3-10 of the Answer under 35 USC 112, first paragraph, for failure to comply with the enablement requirement.

The rejection boils down to whether the specification adequately teaches how to obtain antibodies which will recognize proteonic cancer markers from in vivo sources so that an immunological reaction can be made to occur to indicate a positive screening test result, and whether the specification adequately teaches how to determine whether the immunological reaction occurring in the analytical step is sufficiently strong to be indicative of a positive screening.

For reasons stated in the Brief, s' claims do not stand or fall together, claim 16 being more specific than claim 1 as to the types of cancer cells employed and the ELISA titer required to indicate a positive screening result.

This invention relates to screening people for cancer. Each of the claims is directed toward "A non-invasive cancer screening method."

The difference between a screening method and a diagnostic method is that a screening method assigns nonsymptomatic patients to a risk category, whereas a diagnostic method determines whether or not a patient has a disease. The arguments set forth on page 6 of the Answer relate largely to diagnostic methods, which is not the nature of the claimed invention. By focussing on diagnostic methods, rather than screening methods, the examiner sets the bar for enablement too high and the rejection should be reversed on this basis alone.

When the claimed screening method is carried out, a patient that has a test result over a predetermined value (for example, 1000) is at higher risk for cancer than a patient that has a test result of less than a predetermined value (for example, less than 1000). As is well known to those skilled in the art, (persons possessing doctorate degrees and several years of experience) the predetermined value can be moved higher to reduce the number of false positive test results, or lower to reduce the number of false negative test results. There is no magic number, and the failure

of the specification to provide one does not establish a meritorious case of nonenablement. Based on the description and examples, and the skill level of the art, a suitable predetermined value for the screening test cutoff can be determined without unreasonable experimentation (Claims1-3, 8-10, 11-12 and 20-24), and need not be determined at all for claims 16-17, which state that it is to be 1:1,000.

It is further argued, beginning on page 7 of the Answer, essentially that the specification is not enabling for detecting proteonic cancer markers from *in vivo* sources, since the antibodies used for detection are formed against proteonic cancer markers from *in vitro* sources. The argument draws heavily on analogy with the statement "Cell lines are imperfect predictors of drug efficacy in de novo tumors" appearing on page 9 of the Answer.

However, the claimed method is non-analogous to (non-antibody-based) cancer drug efficacy, since the invention is not an anti-cancer drug or its use, but rather a cancer screening method. By defining the state of the art as cancer drug efficacy, the examiner sets an irrelevant or too high of standard for enablement. Tumors are not being killed in the inventive methods. They are instead being indirectly detected by their slate of PCM emissions. No argument has been advanced by the examiner to

indicate why the slate of PCM emissions from *in vivo* tumors would be so different from the slate of PCM emissions from corresponding *in vitro* tumors that the antibodies formed against mixtures of PCM emissions from *in vitro* tumors wouldn't recognize enough of the PCM emissions from *in vivo* tumors to react immunologically with them. That one skilled in the art might not be able to predict whether a particular PCM is produced by both *in vivo* and *in vitro* cancer cells misses this point. Because of the way the slate of antibodies is produced, there are many opportunities for immunological reactions to occur. Further, the inventive method using a mixture or slate of anti-PCMs derived from *in vitro* sources is demonstrated in the examples to detect PCMs from *in vivo* sources.

In view of the forgoing remarks, it is submitted that the rejection for lack of enablement is in error and should be reversed.

Rejection 2--Lack of written description

Claims 1-3, 8-12, 16-18, 20 and 24 stand rejected as set forth on pages 10-13 of the Answer for failure to comply with the written description requirement.

The basis for the rejection is stated on page 11 of the Answer, to wit:

> "One of skill in the art can reasonably conclude that applicant was not in possession of a genus of 'a mixture from different types of cancer cells containing proteonic cancer markers identified and markers not yet identified' at the time the invention was filed."

The purpose of the written description requirement is to allow persons of ordinary skill in the art to recognize that the inventor invented what is claimed. In Lilly, whether or not the specification demonstrated possession of the claimed genus of compositions was the determinative issue, since a genus of compositions was being claimed. Here, a method is being claimed, and whether the specification demonstrates possession generically of one of the workpieces employed in the claim is not determinative of whether possession of the method is reasonably shown.

It is not necessary to know what the markers are in order to practice the claimed

method. One must know how to obtain and use the markers to make an antibody-containing reagent which is used in the screening test. Since the examples show obtaining and using the markers to make the antibody-containing reagent, and successfully using the reagent to conduct screening for in vivo derived cancer markers in saliva, one skilled in the art would conclude from the examples that Appellants had possession of a genus broader in scope than the species actually used. There is simply no reason to doubt that PCMs from a wide range of cancer cells can be employed to make antibodies and carry out the method invention.

For reasons stated in the Brief, Appellants' claims do not stand or fall together, claim 16 being more specific than claim 1 as to the types of cancer cells in the mixture.

Claim 1 recites: "providing a mixture of proteonic cancer markers from different types of cancer cells, said mixture containing proteonic cancer markers identified and markers not yet identified." Different types of cancer cells were known to the art. It was known that cancer cells produced proteonic cancer markers, some of which were known and others not. What was not known was putting these proteonic cancer markers in a mixture, forming a slate of antibodies against the

mixture, and then using the slate of antibodies to screen for cancers, particularly against PCMs found in saliva. The level of skill in the art is mostly likely a doctorate degree and several years of research experience. Making a mixture of known materials is well within the level of skill. Furthermore, the specification provides a description of 4 "species" within the "genus" and demonstrates operability for them, and these are set forth in claim 16 as "a mixture of proteonic cancer markers obtained from breast, liver, colon, and ovarian cancers, said mixture containing proteonic cancer markers identified and markers not yet identified" so at least claim 16 should be in compliance. Because of these factors, and because of the disclosure of representative species within the scope of the claims, it is submitted that all claims are in compliance with the written description requirement.

Further, the specification demonstrates in the examples that Appellants had possession of an embodiment of the invention within the scope of the claims. How to make the markers is taught. How to use the markers to make the necessary antibodies is taught. How to use the antibodies to conduct a screening test is taught. No reason has been advanced to doubt that Appellants failed to do what is described in the examples, and the examples fairly support the constructive reduction to practice of that which is described in the specification. The specification as a whole

would allow one of ordinary skill in the art to recognize that Appellants invented what is claimed.

Still further, the level of skill and knowledge in the art is such that one would be able to follow the detailed steps of the claimed methods. The practice of the method requires no knowledge of the structures of a compound that would predictably result in the desired activity; rather, the claimed invention is a screening method, not the compounds screened for, or the compounds employed in the screening, or the compounds employed to make the screening compounds. Thus, one of ordinary skill in the art would conclude that Appellants were in possession of the claimed method of screening for cancers at the time of filing.

The Lilly case is not on point, as the unsupported (and un-described) "genus" there was a generically claimed, inadequately characterized, composition of matter which was asserted to be novel. The present claims are methods, and the materials employed are known and/or obtainable from known materials using the teaching of the specification and are characterized functionally and by way of example, and are not claimed.

In view of the forgoing remarks, it is submitted that the rejection for lack of a written description is in error and should be reversed.

REPLY TO "RESPONSE TO ARGUMENT" IN EXAMINER'S ANSWER

It is asserted on page 15 of the Answer that the Examples demonstrate a false positive rate "of at least 25%" when a cut-off of 1000 is used. The showing of the examples was discussed in Appellant's main brief. If the examiner is correct in this assertion, it is submitted that a false positive rate of 25% in a screening test is acceptable since the purpose of a screening test is to divide the population into low risk and high risk groups, and further that it would be obvious to one skilled in the art how to reduce the false positive rate to lower than 25% if such was desired. It is further noted that the argument is only applicable to claims 16-17.

On pages 18-19 of the Answer, the Examiner argues that antibodies made against *in vitro* or *in vivo* sources of cancer cells will not necessarily bind to cancer markers found in a patient. To this, Appellants respond that is why mixtures are used, to increase the probability that detectable binding will occur. The examiner asserts that the majority of proteins in cancer cells are not unique and thus their presence is not indicative of cancer. To this, Appellants respond that is why test results above a

predetermined value are necessary for a positive test result. The Examiner further asserts that a marker for one cancer could not predictably be expected to be a marker for another cancer. To this, Appellants respond that mixtures of markers are employed to overcome this. The Examiner still further asserts that the markers indicative of cancer must be found in the saliva in order for the test to be operative. To this, Appellants responds that the examples demonstrate that the markers are detectably found in saliva.

It is argued on page 21 of the Answer that "Although one of skill in the art could make cell extracts that have a mixture of proteins and other cellular constituents that may or may not be cancer markers, the claims are drawn to providing a mixture of proteonic cancer markers from different cancer cells or cancers said, mixtures containing proteonic cancer marks identified and markers not yet identified, not providing a cell extract." Appellants respond that all solutions are mixtures, but not all mixtures are solutions. Therefore, to provide a cell extract is to provide a mixture, and the necessary constituents of the mixture are described adequately to carry out the invention.

On page 24 of the answer, the Lilly case is revisited. It is emphasized in response

that in Lilly, the composition claims (to human insulin cDNA, mammalian insulin cDNA and vertebrate insulin cDNA) were not adequately supported by the disclosure of cDNA for rat insulin. From the facts, the cDNA of rat insulin is not an example of the cDNA of human insulin claim nor does it by itself constitute disclosure of a sufficient number of species to support claims directed broadly to mammalian insulin cDNA or vertebrate insulin cDNA. The purpose of the written description requirement is to allow persons of ordinary skill in the art to recognize that the inventor invented what is claimed, In re Gosteli, 10 USPQ2d 1614 (Fed. Cir. 1989), and in Lilly there was simply not enough description to enable this. In the instant case, the examples, written description, and logic support the claims.

On page 24 of the Answer, the examiner's assertion that "without a description of said markers one of skill in the art would not be able to provide such markers" cannot be substantiated. Appellants provided the markers without knowledge of their exact description and disclosed to others how they could do the same.

The examiner also asserts on page 25 that ". . .although one could screen for cancer markers, screening assays are not sufficient to describe an invention because 35 USC 112 requires that the specification contains a written description so that one

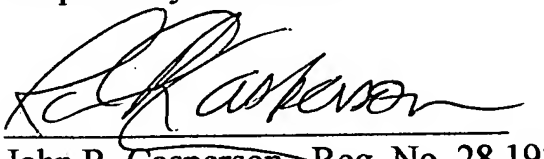
can make and use the invention, not screen for the invention." The comment ignores the claims, which are directed toward screening, which has utility in and of itself.

The examiner asserts, beginning at the bottom of page 24, that "it is unclear how one of skill in the art would recognize that he or she is in possession of a marker not yet identified as the marker is, by definition, not identified." In response, it is not markers which are being claimed, but rather a method which employs them. The issue is whether possession of the method has been demonstrated. As previously discussed, it is not necessary to know the identity of the markers in order to carry out the invention.

CONCLUSION AND SIGNATURE BLOCK

In view of the forgoing arguments, reversal of all grounds of rejection is requested.

Respectfully submitted:



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